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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/543,004	10/11/2006	Martial Ruat	1169-038	2440

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EXAMINER	
SZNAIDMAN, MARCOS L	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
12/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/543,004	RUAT ET AL.	
	Examiner	Art Unit	
	MARCOS SZNAIDMAN	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicant's reply filed on October 8, 2009.

Status of Claims

Cancellation of claims 16-38 and addition of claims 39-48 is acknowledged.

Claims 39-48 are currently pending and are the subject of this office action.

Claims 39-48 are presently under examination.

Priority

The present application is a 371 of PCT/FR04/00151 filed on 01/22/2004, and claims priority to foreign application: FRANCE 03 00646 filed on 01/22/2003.

Rejections and/or Objections and Response to Arguments

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated (Maintained Rejections and/or Objections) or newly applied (New Rejections and/or Objections, Necessitated by Amendment or New Rejections and/or Objections not Necessitated by Amendment). They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103 (New Rejection Necessitated by Amendment)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 39-42 and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haak et. al. (The Lancet (1990) 336:124-125, cited by Applicant, cited in prior office action) in view of Goodman and Gilman's The Pharmacological Basis of Therapeutics (Tenth Edition (2001), McGraw Hill, pages 5-6 and 24-29).

Claim 39 recites a method of modulating a Hedgehog protein signaling pathway in a mammal, which comprises administering to the mammal an amount of RU486 (mifepristone) or an acid addition salt thereof effective to treat tumors linked to hyperactivation of the Hedgehog pathway, wherein the tumors are selected from the group consisting of medulloblastomas, gliuoblastomas, oligodendrogliomas, basal cell carcinomas, etc.

Claim interpretation: for the purpose of this examination, claim 39 is being interpreted as follows: a method of modulating a Hedgehog protein signaling pathway in a mammal, which comprises administering to the mammal an amount of RU486 (mifepristone). The amount of RU486 is such as it will be effective to treat tumors linked to hyperactivation of the Hedgehog pathway. However, claim 39 is not being interpreted as a method of treating tumors linked to hyperactivation of the Hedgehog pathway.

For claim 39, Haak teaches a method of treating meningioma (a type of nervous tissue tumor) comprising administering to the patient an oral dose of mifepristone (see page 125 left column, first paragraph). Haak further teaches the administration of mifepristone at a dose of 200 mg per day for 6 moths followed by 400 mg daily for a further month (see page 125 left column).

While Haak does not teach "modulating a Hedgehog protein signaling pathway", the recitation has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). In other words, what is claimed is: "a method comprising administering to a mammal an effective amount of mifepristone", which is what Haak is teaching.

Haak does not teach an amount of RU486 that is effective to treat tumors linked to hyperactivation of the Hedgehog pathway, wherein the tumors are selected from the group consisting of medulloblastomas, gliuoblastomas, oligodendrogliomas, basal cell carcinomas, etc. However Goodman and Gilman's teach that dosage regimen optimization is routine in the pharmaceutical art. For example on pages 27 and 28 under the heading: Individualizing dosage, the authors mention that: "A rational dosage regimen is based on knowledge of pharmacokinetic parameters (F, CL, Vss and t1/2)

and some information about rates of absorption and distribution of the drug". They also teach: "Individualization of the dosage regimen to a particular patient is, therefore, critical for optimal therapy. The pharmacokinetic principles, described above, provide a basis for modifying the dosage regimen to obtain a desired degree of efficacy with a minimum of unacceptable adverse effects."

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to further modify the dosages taught by Haak with the motivation of determining the optimal amount of RU486 required for optimal therapy for a particular patient, thus resulting in the practice of claim 39 with a reasonable expectation of success.

Claim 40, further limits claim 39, wherein said effective amount of RU486 is administered orally or sublingually.

For claim 40, Haak further teaches the oral administration of RU486 (see page 125).

Claim 41 further limits claim 39, wherein said effective amount of RU486 is administered parentally.

Claim 42, further limits claim 39, wherein said effective amount of RU486 is administered locally.

For claims 41-42 Goodman and Gilman's teach that different forms of administration, like parenteral (see page 5) are standard practice in the pharmaceutical art.

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to administer RU486 by different routes in order to better suit a particular patient's need.

Claim 46 further limits claim 40, wherein said effective amount administered is from 100 mg to 1 g per day for an adult human.

For claim 46, Haak further teaches the administration of mifepristone at a dose of 200 mg per day for 6 moths followed by 400 mg daily for a further month (see page 125 left column). These dosages clearly overlap with the dosages of the instant claim 46.

Haak does not teach the exact same dosages of the instant claims. However, MPEP 2144.05 states: In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim,* 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). Thus resulting in the practice of claim 46 with a reasonable expectation of success.

2) Claims 43-45 and 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haak et. al. (The Lancet (1990) 336:124-125, cited by Applicant, cited in prior office action) in view of Goodman and Gilman's The Pharmacological

Basis of Therapeutics (Tenth Edition (2001), McGraw Hill, pages 5-6 and 24-29) as applied to claims 39-42 and 46 above, and further in view of Bastin et. al. (Organic Process Research Development (2000) 4:427-435).

Claims 43-45 and 47-48 further limit claim 39, wherein an acid addition salt is administered (claim 43), wherein the acid addition salt is a salt of an inorganic acid (claim 44), wherein the inorganic acid addition salt is a salt pf hydrochloric acid, hydrobromic acid, nitric acid, sulfuric acid or phosphoric acid (claim 47), wherein the acid addition salt is a salt of an organic acid (claim 45), wherein the organic acid addition salt is a salt of acetic acid, benzoic acid, maleic acid, fumaric acid, succinic acid, tartaric acid, citric acid or aspartic acid (claim 48).

Haak in view of Goodman and Gilman's teach all the limitations of claims 43-45 and 47-48, except for the specific salts. However Bastin teaches that making salts of known drugs is standard practice in the pharmaceutical art (see abstract) in order to improve the pharmacokinetic properties of the drug. Among the most common salts they teach: hydrochloride, hydrobromide, acetate, benzoate, etc. (see Table 1 on page 428).

At the time of the invention, it would have been *prima facie* obvious for a person of ordinary skill in the art to administer any salt of RU486, since the prior art teaches that salt formation of known drugs is routine practice in the pharmaceutical art, the motivation being increase in the solubility and bioavailability of the drug, thus resulting in the practice of claims 43-45 and 47-48 with a reasonable expectation of success.

Withdrawn Rejections and/or Objections

Claims objected.

Due to applicant's cancellation of claim 27, the objection is now moot.

Objection of claim 27 is withdrawn.

Claims rejected under 35 USC 112, second paragraph.

Due to applicant's cancellation of claim 28, the 35 USC 112, the second paragraph rejection is now moot.

Rejection under 35 USC 112, second paragraph is withdrawn.

Claims rejected under 35 USC 102 (b)

Due to Applicant's cancellation of claims 16-38, the 102(b) rejections based on Haak et. al., Reiner et. al. and Gettys et. al. are now moot.

Rejections under 35 USC 102(b) are withdrawn.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCOS SZNAIDMAN whose telephone number is (571)270-3498. The examiner can normally be reached on Monday through Thursday 8 AM to 6 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARCOS SZNAIDMAN/
Examiner, Art Unit 1612
November 30, 2009

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612